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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/993,647	11/27/2001	Bernd Riedl	BAYER 18A	1010

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EXAMINER	
RAO, DEEPAK R	

ART UNIT	PAPER NUMBER
1624	

NOTIFICATION DATE	DELIVERY MODE
07/26/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

docketing@mwzb.com

Office Action Summary	Application No.	Applicant(s)	
	09/993,647	RIEDL ET AL.	
	Examiner	Art Unit	
	Deepak Rao	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 June 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *74,81,87,93,100-104,106-109,111-115 and 117-119* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4,81,87,93,100-104,106-109,111-115 and 117-119* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *20100601 (2 statements)*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 1, 2010 has been entered.

Claims 74, 81, 87, 93, 100-104, 106-109, 111-115 and 117-119 are pending in this application.

Information Disclosure Statement

Receipt is acknowledged of the Information Disclosure Statements filed on June 1, 2010 and copies are enclosed herewith. References #**M1**, IR 26555 (page 22 or 56) and #**O1**, LR 6124 (page 23 of 56) were crossed-off because these references did not have a publication date, which is required. 37 CFR 1.198(b).

The following rejections are maintained:

Claims 74, 81, 87, 93, 100-103, 106-109, 111-114 and 117 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for the treatment of carcinoma of the colon or villous colon adenoma (based on the *in vitro* treatment of the tumor cell lines HCT116 and DLD-1 provided in the specification), does not reasonably provide enablement for a method for the treatment of all types of solid tumors, carcinomas,

myeloid disorders or adenomas; or a method for inhibiting RAF-kinase in a human or mammal. The reasons of the previous office action(s) are incorporated here by reference.

Applicant's arguments have been fully considered but they have not been found to be persuasive. The references cited by the applicant (i.e., Awada (2005); Clark (2005); Moore (2005); Escudier (2007); etc.) are not state of the art references as of the filing date of the instant application. Applicant has not provided any reference(s) that forms sufficient evidence that claimed uses were art-recognized based on activity relied on at the time of applicants' effective filing date. MPEP 2164.05(a). As explained in the previous office action, the state of the art is not indicative of the fact that treatments of all types of diseases encompassed by the instant claims are conventional or well known.

Applicant relies on the state of the art references, Monia, Kolch, Daum and Fridman, and argues that 'the references show the correlation between the inhibition of raf kinase with the inhibition of the growth of a variety of solid tumor types'. Contrary to applicant's arguments, the state of the art references do not establish a therapeutic method for the treatment of all types of solid tumors, carcinomas, myeloid disorders or adenomas generally. As explained in the previous office action, the state of the art is not indicative of the fact that treatments of all types of diseases encompassed by the instant claims are conventional or well known. The cited references are too speculative and invite further research into treatment of cancer diseases. For example, Monia at page 668 provides that "the emergence of novel therapies that specifically reverse the oncogenic effect of these gene products has generally been slow". All references provided as evidence of enabling disclosure present no evidence that the claimed compounds actually have activity in treating all types of solid tumor, carcinoma, myeloid disorders or

adenoma. There is no evidence of record that the claimed compounds are actually efficacious in treating all types of solid tumor, carcinoma, myeloid disorders or adenoma; or inhibit RAF-kinase generally.

Applicant's arguments based on the state of the art references – Monia, Kolch, Daum, Fridman, etc. have been fully considered but not deemed to be persuasive. However, the cited references do not cure the deficiencies of the specification. Considered separately or together, these references invite further research into the treatment of solid tumor, carcinoma, myeloid disorder, adenoma, etc. through inhibition of RAF-kinase.

Applicant cites *In re Brana* and argues that 'there is no requirement that an applicant provide any working examples'. Applicant's reliance on the *Brana* decision is erroneous since the facts were different in more than one respect from the instant case. In *Brana*, the compounds on appeal were of a much narrower scope and there were no method claims. Said compounds were similar in structure to compounds displaying *in vivo* anti-tumor activity based on art-recognized *in vivo* tests and also tested favorably in an *in vivo* test. Thus, contrary to *Brana* it is not evident that at the time of applicant's effective filing that RAF kinase inhibitors having such a diversity of substituents on analogous urea compounds are well known for treating any disease mediated by RAF kinase urged treatable based simply on assay testing relied on herein or for treating solid cancer, adenoma or melanoma generally.

The guidance in the specification is limited to an *in vitro* cell proliferation assay showing inhibition of two colon cancer cell lines; and summary instructions relating to an *in vivo* assay in mice that can be performed to determine the inhibition of a human colon adenocarcinoma cell line (see pages 94-96). There is no evidence of record how the provided data is directly involved

in the pathogenesis of all types of solid tumors, carcinoma, myeloid disorders or adenoma and/or that simply inhibiting RAF-kinase will lead to treatment of all of these diseases. It is not routine for one skilled in the art to synthesize, purify, screen for RAF-kinase inhibition, and test for anticancer activity of the claimed compounds.

Applicant argues that 'claim 117 is directed to a method of inhibiting raf-kinase in a human or other mammal and not a method of treatment claim for any condition, including cancer'. As previously provided, the claim is directed towards 'a method for inhibiting RAF-kinase in a human or mammal' - which involves administering of the compound to human or mammal and therefore reaches through to the treatment of all types of diseases associated with RAF-kinase. The findings and conclusions in the cited publications are with respect to inhibition of RAF kinase and the application of such activity for specific types of cancerous growth. The development of the most efficacious strategy for the treatment of cancers is based on understanding the underlying mechanisms of carcinogenesis. This includes the knowledge that the carcinogenic process is a multi-step, multi-mechanism process and that no two cancers are alike, in spite of some apparent universal characteristics, such as their inability to have growth control, to terminally differentiate, to apoptose abnormally and to have an apparent extended or immortalized life span. Since tumor promotion phase involves multiple mechanisms, there is no existence of a single therapeutic approach. The evidence of record does not disclose any known compounds of similar structure, which have been demonstrated to inhibit RAF-kinase generally and thereby treat all diseases mediated by raf kinase; or treat all types of solid tumors, carcinomas, myeloid disorders or adenomas, when the compounds are administered to a human or a mammal.

Allowable Subject Matter

Claims 104, 115, 118 and 119 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deepak Rao whose telephone number is (571) 272-0672. The examiner can normally be reached on Monday-Friday from 8:00am to 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson, can be reached at (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Deepak Rao/
Primary Examiner
Art Unit 1624

July 21, 2010